

Claims:

1. A solid controlled release pharmaceutical formulation for once daily administration comprising
a core comprising venlafaxine, polyvinylpyrrolidone, a low viscosity hydrophilic polymer and a high viscosity hydrophilic polymer; and
a polymeric coating comprising a water high permeable polymer, and a water low permeable polymer.
2. The formulation of claim 1 wherein venlafaxine is in a form of venlafaxine hydrochloride.
3. The formulation of claim 1 and 2 wherein venlafaxine is in amorphous form.
4. The formulation of claim 1 wherein the amount of venlafaxine is from 10 to 400 mg.
5. The formulation of claim 1 wherein the amount of venlafaxine is from 37,5 to 150 mg.
6. The formulation of claim 1 wherein the amount of venlafaxine is 75 mg.
7. The formulation of claim 1 wherein the amount of venlafaxine is 150 mg.
8. The formulation of claim 1 wherein the low viscosity hydrophilic polymer and the high viscosity hydrophilic polymer in the core are selected from cellulose ethers.
9. The formulation of claim 1 wherein the low viscosity hydrophilic polymer and the high viscosity hydrophilic polymer in the core are selected from the group consisting of methylcellulose, ethylcellulose, hydroxyethylcellulose,

propylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose or carboxymethylcellulose.

10. The formulation of claim 1 wherein the low viscosity hydrophilic polymer and the high viscosity hydrophilic polymer in the core are a low viscosity hydroxypropylmethylcellulose and a high viscosity hydroxypropylmethylcellulose.

11. The formulation of claim 1 wherein the ratio between polyvinylpyrrolidone and the low viscosity hydrophilic polymer in the core is from 10:1 to 1:10.

12. The formulation of claim 1 wherein the ratio between polyvinylpyrrolidone and the low viscosity hydrophilic polymer in the core is from 1:3 to 3:1.

13. The formulation of claim 1 wherein the ratio between the low viscosity hydrophilic polymer and the high viscosity hydrophilic polymer in the core is from 10:1 to 1:3.

14. The formulation of claim 1 wherein the ratio between the low viscosity hydrophilic polymer and the high viscosity hydrophilic polymer in the core is from 3:1 to 1:1

15. The formulation of claim 1 wherein the water high permeable polymer in the coating is selected from the group consisting of methylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose, methacrylate aminoester copolymer, high permeable poly (ethylacrylate, methylmethacrylate) trimethylammoniummethylemethacrylate chloride.

16. The formulation of claim 1 wherein the water high permeable polymer in the coating is selected from the group consisting of hydroxypropylcellulose, hydroxypropylmethylcellulose and high permeable poly

(ethylacrylate, methylmethacrylate)
trimethylammoniummethylmethacrylate chloride.

17. The formulation of claim 1 wherein the water low permeable polymer in the coating is selected from ethylcellulose, cellulose acetate phthalate, methacrylic acid copolymers, polyvinyl acetate phthalate, cellulose acetate trimellitate, hydroxypropylmethylcellulose phthalate and low permeable poly (ethylacrylate, methylmethacrylate)
trimethylammoniummethylmethacrylate chloride.

18. The formulation of claim 1 wherein the water low permeable polymer in the coating is selected from ethylcellulose, hydroxypropylmethylcellulose phthalate and low permeable poly (ethylacrylate, methylmethacrylate)
trimethylammoniummethylmethacrylate chloride.

19. The formulation of claim 1 wherein the combinations of water high permeable and water low permeable polymers is selected from: hydroxypropylmethylcellulose and hydroxypropylmethylcellulose phthalate, hydroxypropylcellulose and hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose and ethylcellulose, hydroxypropylcellulose and ethylcellulose, hydroxypropylmethylcellulose and polyvinyl acetate phthalate, hydroxypropylcellulose and polyvinyl acetate phthalate, high permeable poly (ethylacrylate, methylmethacrylate)
trimethylammoniummethylmethacrylate chloride and low permeable poly (ethylacrylate, methylmethacrylate)
trimethylammoniummethylmethacrylate chloride.

20. The formulation of claim 1 wherein the combination of water high permeable and water low permeable polymers is selected from the following combinations:
hydroxypropylmethylcellulose and hydroxypropylmethylcellulose phthalate, hydroxypropylcellulose and ethylcellulose, hydroxypropylmethylcellulose and ethylcellulose, high permeable

poly (ethylacrylate, methylmethacrylate)
trimethylammoniummethylmethacrylate chloride and low permeable
poly (ethylacrylate, methylmethacrylate)
trimethylammoniummethylmethacrylate chloride.

21. The formulation of claim 1 wherein the ratio between the water high permeable and the water low permeable polymer in the coating is from 10:1 to 1:5.

22. The formulation of claim 1 wherein the ratio between the water high permeable and the water low permeable polymers in the coating is from 3:1 to 1:3

23. The formulation of claim 1 wherein the coating represents 1 to 15 wt.% of the total weight of the formulation.

24. The formulation of claim 1 wherein the coating further comprises a plasticizer selected from the group consisting of acetyl tributyl citrate, acetyl triethyl citrate, acetylated fatty acid glycerides, castor oil, dibutyl phthalate, diethyl phthalate, diethyl sebacate, dibutyl sebacate, dimethyl phthalate, glycerol, glycerol monostearate, glyceryl triacetate, polyethylene glycols, polyoxyethylene/polyoxypropylene copolymers, propylene glycol, tributyl citrate, triethyl citrate.

25. The formulation of claim 24 wherein the plasticizer is triethyl citrate.

26. A process for the preparation of a solid controlled release pharmaceutical formulation comprising the steps of:

dissolving venlafaxine and polyvinylpyrrolidone in an organic solvent,

applying the resulting solution onto low viscosity polymer,

homogeneously mixing the obtained granulate with a high viscosity polymer, and

compressing the granulate to obtain a core which is then coated with a polymeric coating comprising a water high permeable polymer and a water low permeable polymer.

27. The process of claim 26 wherein venlafaxine in amorphous or in polymorphous form is dissolved in an organic solvent.

28. The process of claims 26 or 27 wherein the organic solvent is selected from the group consisting of ethanol, methanol, isopropyl alcohol, n-butyl alcohol, acetone, diethyl ether, ethyl acetate, isopropyl acetate, methyl acetate, dichloromethane, chloroform and mixtures thereof.

29. The process of claim 26 or 28 wherein the organic solvent is ethanol.

30. The process of claim 26 wherein the film coating is applied from organic solvent or aqueous media.

31. The process of claim 26 wherein the low viscosity hydrophilic polymer and the high viscosity hydrophilic polymer in the core are selected from cellulose ethers.

32. The process of claim 26 wherein the low viscosity hydrophilic polymer and the high viscosity hydrophilic polymer in the core are selected from the group consisting of methylcellulose, ethylcellulose, hydroxyethylcellulose, propylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose or carboxymethylcellulose.

33. The process of claim 26 wherein the low viscosity hydrophilic polymer and the high viscosity hydrophilic polymer in the core are a low viscosity hydroxypropylmethylcellulose and a high viscosity hydroxypropylmethylcellulose.

34. The process of claim 26 wherein the water high permeable polymer in the coating is selected from the group consisting of

methylcellulose, hydroxypropylcellulose,
hydroxypropylmethylcellulose, hydroxyethylcellulose,
methacrylate aminoester copolymer, high permeable poly
(ethylacrylate, methylmethacrylate)
trimethylammoniummethylmethacrylate chloride.

35. The process of claim 26 wherein the water high permeable polymer in the coating is selected from the group consisting of hydroxypropylcellulose, hydroxypropylmethylcellulose and high permeable poly (ethylacrylate, methylmethacrylate) trimethylammoniummethylmethacrylate chloride.

36. The process of claim 26 wherein the water low permeable polymer in the coating is selected from ethylcellulose, cellulose acetate phthalate, methacrylic acid copolymers, polyvinyl acetate phthalate, cellulose acetate trimellitate, hydroxypropylmethylcellulose phthalate and low permeable poly (ethylacrylate, methylmethacrylate) trimethylammoniummethylmethacrylate chloride.

37. The process of claim 26 wherein the water low permeable polymer in the coating is selected from ethylcellulose, hydroxypropylmethylcellulose phthalate and low permeable poly (ethylacrylate, methylmethacrylate) trimethylammoniummethylmethacrylate chloride.